

REVISED CLAIM SET

1. An apparatus for growing cells comprising at least one bioreactor for cell culture, at least one vessel for culture medium, means for circulating culture medium and/or cell culture, whereby the bioreactor and vessel are in fluid communication, and at least one means for delivery of oxygen wherein the means for delivery of oxygen provides an average dissolved concentration of between about 30% and 90%.
2. An apparatus for growing cells comprising a bioreactor for cell culture, a vessel for culture medium, means for circulating cell culture, means for circulating culture medium, dialysis means in fluid communication with the bioreactor and the vessel, whereby there is a first, cell culture, loop between the bioreactor and the dialysis means, and a second, media replenishment, loop between the vessel and the bioreactor, and in operation dialysis between the culture medium and the cell culture, and at least one means for delivery of oxygen into the cell loop culture wherein the means for delivery of oxygen provides an average dissolved oxygen concentration between about 30% and 90%.
3. The apparatus of Claim 1 or 2, wherein the means for delivery of oxygen provides an average dissolved oxygen concentration between about 40% and 80%.
4. The apparatus of Claim 1, 2 or 3, wherein the means for delivery of oxygen provides an average dissolved oxygen concentration between 50% and 70%.
5. The apparatus of any one of Claim 1 to 4, wherein the means for delivery of oxygen provides an average dissolved oxygen concentration of greater than 40%.
6. The apparatus of any one of Claim 1 to 5, wherein the means for delivery of oxygen provides an average dissolved oxygen concentration of about 60%.

7. The apparatus of any one of Claims 1 to 6, wherein the means for delivery of oxygen comprises a hollow fiber filter oxygenator.
8. The apparatus of any one of Claims 1 to 6, wherein the means for delivery of oxygen comprises means for in-line sparging.
9. The apparatus of any one of Claims 1 to 6, wherein the means for delivery of oxygen comprises means for delivery of at least one oxygen-containing compound that releases dissolved oxygen into cell culture.
10. The apparatus of any one of Claims 1 to 6, wherein the means for delivery of oxygen is positioned upstream of input of circulating cell culture returning to the bioreactor.
11. The apparatus of any one of Claims 1 to 6, wherein the bioreactor and/or the vessel are stirred.
12. The apparatus of any one of Claims 2 to 6, wherein the dialysis means comprises at least one semi-permeable membrane.
13. The apparatus of Claim 12, wherein the semi-permeable membrane comprises at least one hollow fiber filter.
14. The apparatus of Claim 1 or 2, further comprising a means for measuring the physical and/or chemical parameters of the cell culture and/or medium, wherein the means for measuring comprises means for measuring dissolved oxygen concentration, and wherein the dissolved oxygen measurement varies from 30% to 90%.
15. The apparatus of Claim 14, wherein the dissolved oxygen measurement varies from 40% to 80%.
16. The apparatus of Claim 14 or 5, wherein the dissolved oxygen measurement varies from 50% to 70%.
17. The apparatus of Claim 14, 15 or 16, wherein the dissolved oxygen measurement averages about 60%.
18. The apparatus of any one of Claims 14 to 17, wherein the dissolved oxygen measurement varies from high value to low value over about 10 to about 30 minutes.

19. The apparatus of any one of Claims 14 to 18, wherein the dissolved oxygen measurement varies from high value to low value over about 20 minutes.
20. The apparatus of any one of Claims 14 to 19, wherein a plot of the dissolved oxygen measurement as a function of time comprises a sin wave.
21. The apparatus of Claim 14, wherein the means for measuring further comprises means for measuring pH.
22. The apparatus of Claim 14 or 21, wherein the means for measuring further comprises means for measuring temperature.
23. The apparatus of Claim 14, 21, or 22, wherein the means for measuring further comprises means for measuring cell density or amount of cells.
24. The apparatus of any one of Claims 14 to 23, further comprising a means for adjusting physical and/or chemical parameter(s) of the cell culture and/or medium in response to data from the means for measuring.
25. The apparatus of Claim 24, wherein the means for adjusting comprises means for adjusting dissolved oxygen concentration.
26. The apparatus of Claim 24 or 25, wherein the means for adjusting comprises means for adjusting pH.
27. The apparatus of Claim 24, 25 or 26, wherein the means for adjusting comprises means for adjusting temperature.
28. The apparatus of any one of Claims 24 to 27, wherein the means for adjusting comprises means for adjusting dissolved carbon dioxide concentration.
29. The apparatus of any one of Claims 24 to 28, wherein the means for adjusting comprises means for adding a vector in response to a cell density or cell amount measurement.
30. The apparatus of Claim 28, wherein in response to pH measurement(s), dissolved carbon concentration is adjusted.
31. The apparatus of Claim 25, wherein in response to dissolved oxygen measurement(s), dissolved oxygen concentration is adjusted.

32. The apparatus of Claim 30, wherein pH is set to a desired level and carbon dioxide is adjusted when pH varies from the desired level, whereby the oxygen measurement varies periodically as a function of time.
33. A method for growing cells comprising culturing cells in at least one bioreactor whereby there is a cell culture, supplying medium in at least one vessel whereby there is a culture medium, circulating culture medium and/or cell culture, whereby the bioreactor and vessel are in fluid communication and the cell culture and/or medium are in circulation, and delivering oxygen to the cell culture and/or medium wherein the delivering of oxygen provides an average dissolved oxygen concentration of between about 30% and 90%.
34. A method for growing cells comprising culturing cells in a bioreactor whereby there is a cell culture, supplying culture medium in a vessel whereby there is culture medium, circulating the cell culture through a dialysis means, circulating culture medium through the dialysis means, wherein the dialysis means is in fluid communication with the bioreactor and the vessel, whereby there is a first, cell culture, loop between the bioreactor and the dialysis means, and a second, media replenishment, loop between the vessel and the bioreactor, performing dialysis between culture medium and the cell culture, and delivering oxygen into the cell culture loop wherein the delivering of oxygen provides an average dissolved oxygen concentration of between about 30% and 90%.
35. The method of Claim 33 or 34, wherein the delivering of oxygen provides an average dissolved oxygen concentration of between about 40% and 80%.
36. The method of Claim 33, 34 or 35, wherein the delivering of oxygen provides an average dissolved oxygen concentration of between about 50% and 70%.
37. A method of any one of Claims 33 to 36, wherein the delivering of oxygen provides an average dissolved oxygen concentration of greater than about 40%.

38. A method of any one of Claims 33 to 37, wherein the delivering of oxygen provides an average dissolved oxygen concentration of about 60%.
39. The method of any one of Claims 33 to 38, wherein the delivering of oxygen is by means for delivery of oxygen comprising a hollow filter oxygenator.
40. The method of any one of Claims 33 to 38, wherein the delivering of oxygen is by means for delivery of oxygen comprising means for in-line sparging.
41. The method of any one of Claims 33 to 38, wherein the delivering of oxygen is by delivery of at least one oxygen-containing compound that releases dissolved oxygen into cell culture.
42. The method of any one of Claims 33 to 38, wherein the delivering of oxygen is upstream of input of circulating cell culture returning to the bioreactor.
43. The method of any one of Claims 33 to 38, further comprising stirring the cell culture and/or medium.
44. The method of any one of Claims 34 to 38, wherein the dialysis means comprises at least one semi-permeable membrane.
45. The method of Claim 44, wherein the semi-permeable membrane comprises at least one hollow fiber filter.
46. The method of Claim 33 or 34, further comprising measuring physical and/or chemical parameters of the cell culture and/or cell medium and adjusting physical and/or chemical parameters of the cell culture and/or medium in response to data from measuring, wherein the measuring comprises measuring dissolved oxygen concentration, wherein the adjusting comprises adjusting dissolved oxygen concentration and wherein the adjusting includes adjusting the dissolved oxygen concentration so that the dissolved oxygen measurement varies from 30% to 90%.

47. The method of Claim 46, wherein the adjusting includes adjusting the dissolved oxygen concentration so that the dissolved oxygen measurement varies from 40% to 80%.
48. The method of Claim 46 or 47, wherein the adjusting includes adjusting the dissolved oxygen concentration so that the dissolved oxygen measurement varies from 50% to 70%.
49. The method of Claim 46, 47 or 48, wherein the adjusting includes adjusting the dissolved oxygen concentration so that the dissolved oxygen measurement varies averages about 60%.
50. The method of any one of Claims 46 to 49, wherein the adjusting includes adjusting the dissolved oxygen concentration so that the dissolved oxygen measurement varies from high value to low value over about 10 to about 30 minutes.
51. The method of any one of Claims 46 to 50, wherein the adjusting includes adjusting the dissolved oxygen concentration so that the dissolved oxygen measurement varies from high value to low value over about 20 minutes.
52. The method of any one of Claims 46 to 51, wherein a plot of the dissolved oxygen measurement as a function of time comprises a sin wave.
53. The method of any one of Claims 46 to 52, wherein the measuring further comprises measuring pH.
54. The method of any one of Claims 46 to 53, wherein the measuring further comprises measuring temperature.
55. The method of any one of Claims 46 to 54, wherein the measuring further comprises measuring cell density or amount of cells.
56. The method of any one of Claims 46 to 55, wherein the adjusting further comprises adjusting pH to maintain a desired pH.
57. The method of any one of Claims 46 to 56, wherein the adjusting further comprises adjusting temperature to maintain a desired temperature.
58. The method of any one of Claims 46 to 57, wherein the adjusting further comprises adjusting dissolved carbon dioxide concentration.

59. The method of any one of Claims 46 to 58, wherein the adjusting further comprises adjusting dissolved oxygen concentration to maintain a desired dissolved oxygen concentration.
60. The method of any one of Claims 46 to 59, wherein the adjusting further comprises adding a vector in response to a cell density or cell amount measurement.
61. The method of Claim 46, whereby in response to dissolved oxygen measurements, dissolved oxygen concentration is adjusted.
62. The method of Claim 46, whereby in response to pH measurement(s), dissolved carbon dioxide levels are adjusted.
63. The method of Claim 46, wherein the adjusting comprises adjusting pH to a desired level in response to pH measurement(s) by adjusting the dissolved carbon dioxide concentration such that dissolved carbon dioxide concentration is adjusted when pH varies from the desired level, and the dissolved oxygen measurement varies as a function of time.
64. The method of any one of Claims 33 to 63, further comprising collecting the cells.
65. The method of any one of Claims 33 to 64, wherein the cells contain a vector for replication of the vector and/or expression of exogenous nucleic acid molecules.
66. The method of Claim 65, wherein the vector comprises a virus or a recombinant virus.
67. The method of Claim 66, wherein the vector comprises a recombinant baculovirus.
68. A method for producing an expression product from a recombinant vector infected or transfected or inserted into a cell, or for producing a vector infected or transfected or inserted into a cell, comprising performing the method of any one of claims 33 to 67, wherein cells of the cell culture are infected or transfected with or have inserted into them the recombinant vector, or the vector, either prior to or during the method.

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69. The method of Claim 68, wherein the recombinant vector is a recombinant baculovirus and the cells are insect cells.
70. The method of Claim 69, wherein the cells are infected during the method.
71. The method of Claim 68, wherein the cells are CHO cells.
72. The method of Claim 68, further comprising collecting the cells or the expression product or the recombinant vector or the vector.
73. The expression product of Claim 68.

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No. 50-0320.

Respectfully submitted,

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Encs.

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